DEPARTMENT OF HEALTH

# A Response to the Substance Abuse Crisis

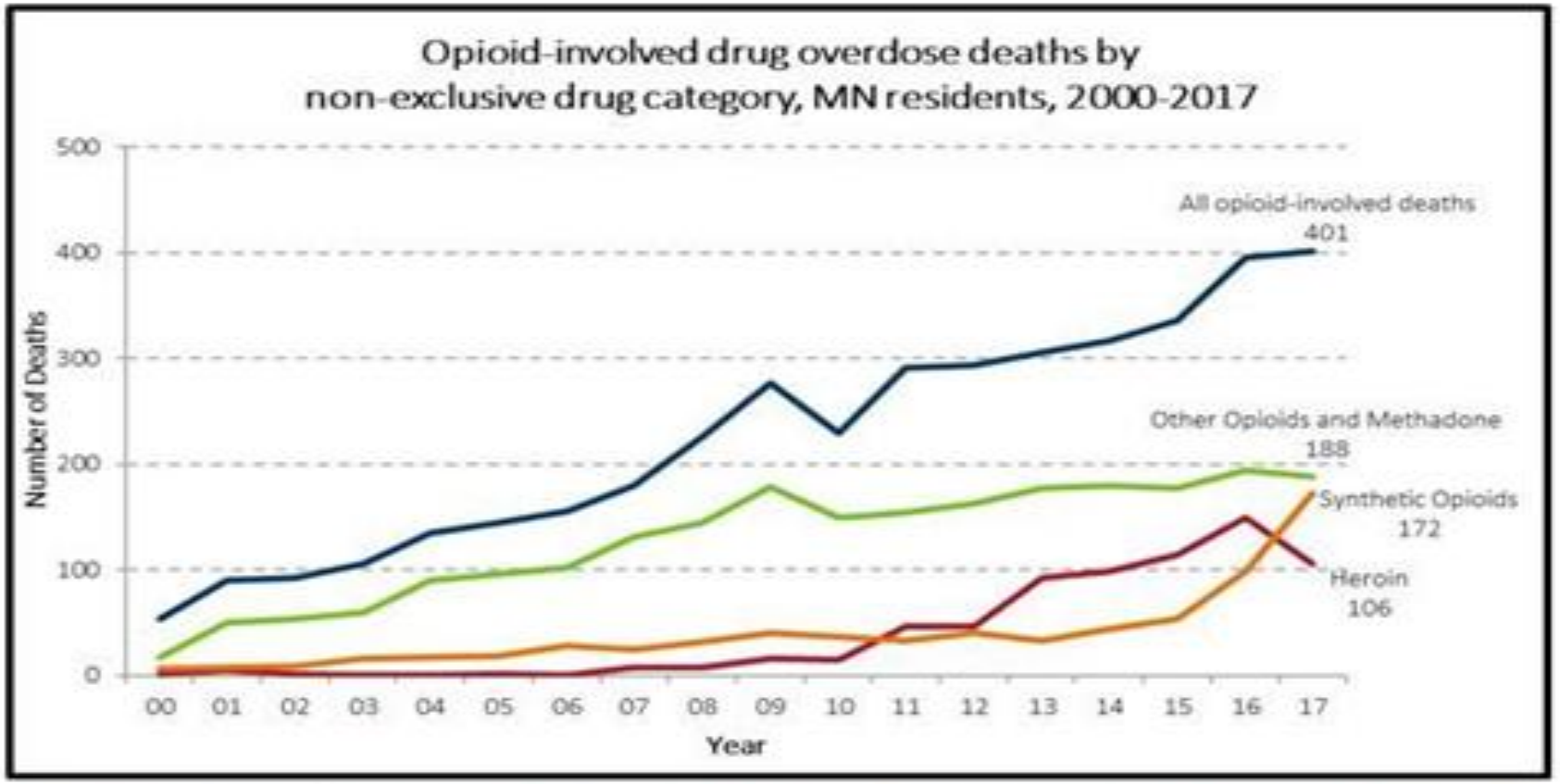
CLIAC Fall Meeting

November 8, 2018

# Overview

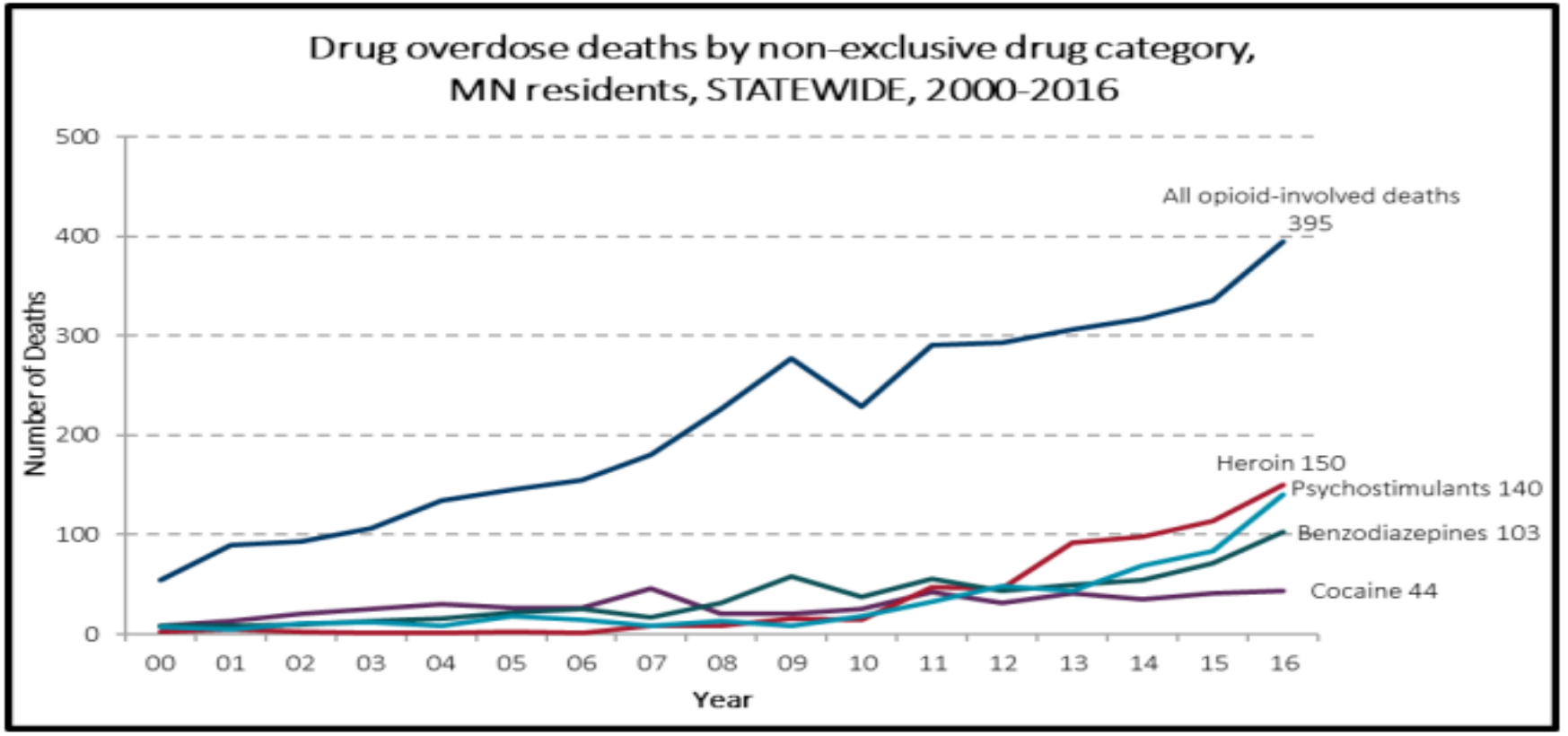
- Minnesota Drug Overdose and Substance Abuse Pilot Surveillance System (MNDOSA)
- Laboratory Component
- Lessons Learned (to date)

# Minnesota Opioid Overdoses




*NOTE: Data are preliminary and likely to change when finalized. Also the category other opioids and Methadone includes prescription opioids.*

# Minnesota Overdose Deaths

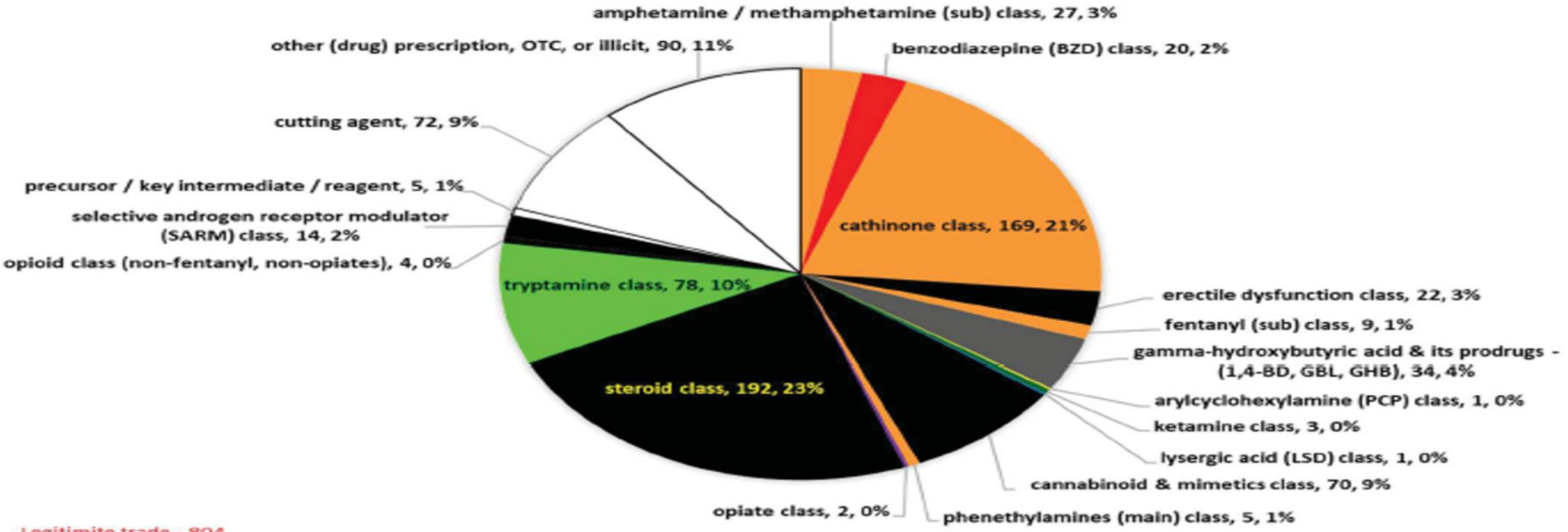



*SOURCE: Minnesota death certificates, Injury and Violence Prevention Section, Minnesota Department of Health, 2000-2016*

*NOTE: Drug categories are non-exclusive*

*NOTE: Psychostimulants includes methamphetamine*

# OPERATION SUSTAIN - AUGUST 2018 BREAKDOWN BY CHEMICAL CLASS




Legitimite trade - 804
Cannot be determined solely by FTIR - 140

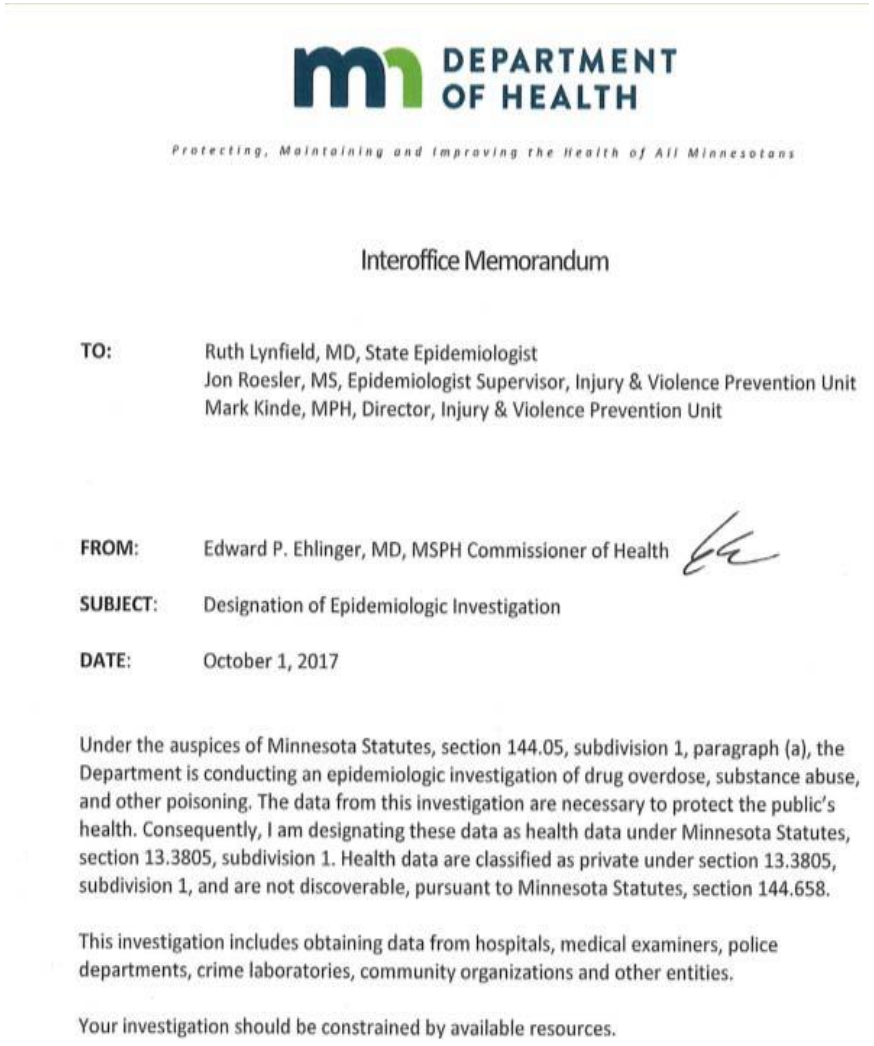
Homeland Security

FOUO/ LES For Official Use Only – Law Enforcement Sensitive

# MDH - PHLD Involvement

- May 2017 – St. Paul, MN reports over 30 individuals having adverse reactions from exposure to a synthetic cannabinoid substance.
  - PHLD was contacted to provide analytical support on fluid samples from those effected.
  - This event brought together our Public Health Laboratory and out Injury and Prevention Division.
- October 2017 – Reports of over 60 people overdosed on synthetic marijuana

# MDH Commissioner's Order



DEPARTMENT OF HEALTH

*Protecting, Maintaining and Improving the Health of All Minnesotans*

Interoffice Memorandum

**TO:** Ruth Lynfield, MD, State Epidemiologist
Jon Roesler, MS, Epidemiologist Supervisor, Injury & Violence Prevention Unit
Mark Kinde, MPH, Director, Injury & Violence Prevention Unit

**FROM:** Edward P. Ehlinger, MD, MSPH Commissioner of Health

**SUBJECT:** Designation of Epidemiologic Investigation

**DATE:** October 1, 2017

Under the auspices of Minnesota Statutes, section 144.05, subdivision 1, paragraph (a), the Department is conducting an epidemiologic investigation of drug overdose, substance abuse, and other poisoning. The data from this investigation are necessary to protect the public's health. Consequently, I am designating these data as health data under Minnesota Statutes, section 13.3805, subdivision 1. Health data are classified as private under section 13.3805, subdivision 1, and are not discoverable, pursuant to Minnesota Statutes, section 144.658.

This investigation includes obtaining data from hospitals, medical examiners, police departments, crime laboratories, community organizations and other entities.

Your investigation should be constrained by available resources.

- Due to the increased abuse of drugs of abuse, the Commissioner of Health, Dr. Edward Ehlinger, ordered the epidemiological investigation of "drug overdose, substance abuse, and other poisoning" in October 2017.
- Memorandum enables the reporting of all patients who meet the case definition to MDH.

# MNDOSA Objectives

- Determine the burden of overdoses/substance abuse seen in select emergency departments and hospitals in Minnesota.
- Identify drug overdose clusters and unusual or atypical clinical presentations.
- Identify substances consumed by individuals to inform future approaches to treatment and prevention.
- Describe the populations most affected to help focus and guide prevention efforts.

# Who will be reported with MNDOSA?

- All patients who are hospitalized or admitted to the ER (regardless of discharge status) where the principal diagnosis is attributed to the recreational use of one or more of the following drug categories (including withdrawal symptoms):

- Traditional **illicit drugs**, including:
  - amphetamines
  - cocaine
  - PCP
  - LSD

- **Opioids** (including heroin)

- **Synthetic**, non-prescription drugs, including:
  - synthetic **cannabinoids** (K2, spice, etc.)
  - synthetic **cathinones** (i.e. bath salts)
  - other synthetic hallucinogens (2-C compounds, NBOMBe or "super LSD", etc.)

- **Prescription drugs**, including:
  - cold medicines
  - barbiturates
  - benzodiazepines
  - other anticonvulsants (Lyrica, gabapentin, etc.)
  - sleep medications
  - stimulants (Adderall, Ritalin, etc.)
  - antidepressants
  - antidiarrheal medications (loperamide, etc.)
  - muscle relaxants

- **Drug combinations**, including:
  - Speedball (cocaine and heroin)
  - Methamphetamine and fentanyl

- **Natural** substances used for recreational purposes, including:
  - marijuana
  - mushrooms
  - psychoactive drugs
  - hallucinogens
  - other herbal substances with intoxicating effects

- Other substances, including:
  - inhalants
  - **other???**

# **How** will reports be made to MNDOSA?

Clinician identifies patients in ER that meet the following criteria:

- Signs/symptoms attributed to drug or substance use/abuse (excluding alcohol only cases)
- Drug or substance use/abuse was recreational, NOT:
  - **Accidental/Unintentional overmedication** (i.e. tried to make up a missed dose, forgot they already took a dose, accidentally doubled the dose, etc.)
  - **Adverse reaction** to medication that was taken as recommended
  - **Accidental ingestion** (i.e. accidental child poisoning, took wrong medication unintentionally, etc.)
- Drug or substance use/abuse was NOT:
  - Intentional overdose (i.e. **suicide attempt**)
  - Assault (i.e. “date rape”, malicious poisoning, etc.)

# MNDOSA Flow Chart

Report **ALL** eligible cases to MNDOSA

Is the case a **"Patient of Special Interest"**?

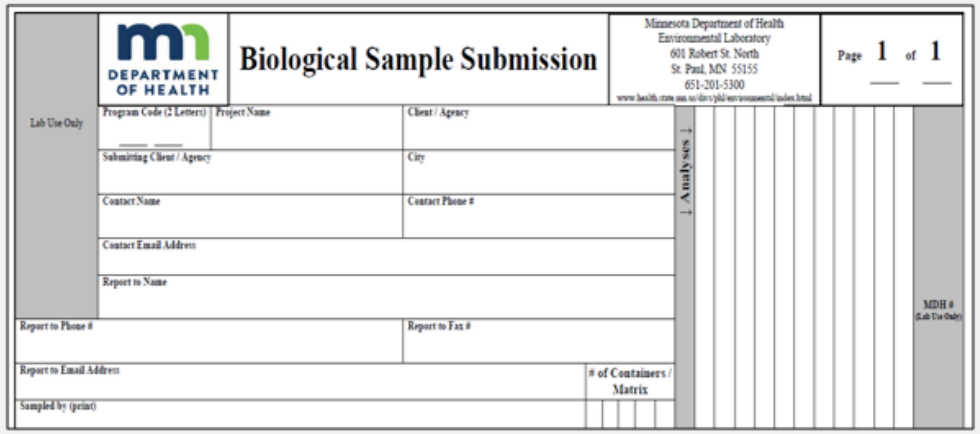
- hospitalized
- unusual clinical presentation
- part of a cluster

If yes:

Were lab specimens collected?

If yes:

Send lab specimens to **MDH Public Health Laboratory**



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**Biological Sample Submission**

Minnesota Department of Health
Environmental Laboratory
601 Robert St. North
St. Paul, MN 55155
651-201-5300

Page 1 of 1

Lab Use Only

Program Code (2 Letter) | Project Name | Client / Agency

Submitting Client / Agency | City

Contact Name | Contact Phone #

Contact Email Address

Report to Name

Report to Phone # | Report to Fax #

Report to Email Address | # of Containers / Matrix

Sampled by (print)

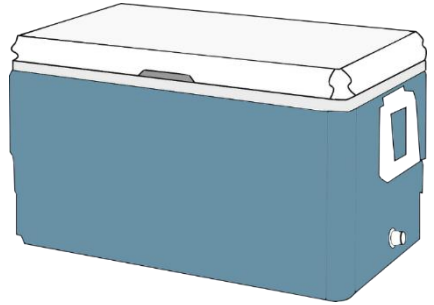
Analyses

MDH # (Lab Use Only)

# Lab Specimen Submission

Submit remaining blood and/or urine specimens for "**Patients of Special Interest**" who had toxicology samples drawn

- Urine
  - Minimum of 5mL
  - Collected in small vials
  - Specimens are to be stored/shipped **frozen** unless delivered the day of collection
- Whole blood
  - Minimum of 1mL
  - Collected in EDTA preserved (purple top) tubes
  - Specimens are to be **kept and shipped cold**



# Lab Specimen Results

- Lab results will be used for **surveillance purposes only**, and reported to:
  - MDH - Injury and Prevention
  - The submitting Hospitals Site Contact
- Lab results **are not used for diagnostic or clinical purposes**
- Lab results **will not go in the patient's medical record**
- Each site will receive an aggregated monthly report, summarizing all patients reported to MNDOSA and aggregate lab results

# Current Participating Sites

**St. Luke's Hospital** – November 2017

**Essentia Health - St. Mary's Medical Center** – November 2017

**Hennepin County Medical Center** – February 2018

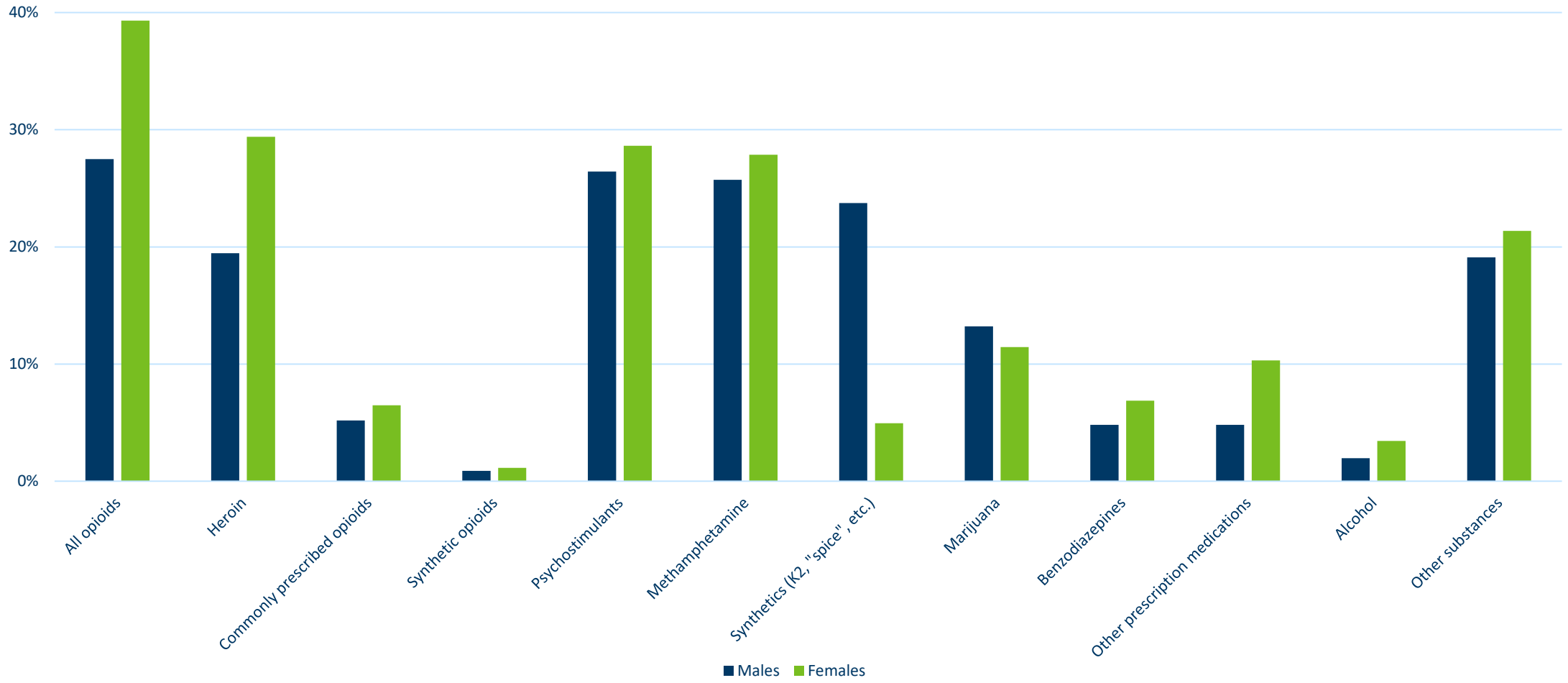
(reports only)

(Four additional Essentia Health Hospitals in NE MN being added.)

# MNDOSA Reports, November 1, 2017 – September 5, 2018

| | |
|---|---|
| Number of ED visits reported | 961 |
| Number of patients reported | 825 |
| "Patients of Special Interest" | |
| Deceased | 6 (<1%) |
| Hospitalized | 221 (23% of all visits) |
| Atypical clinical presentation | 57 (6% of all visits) |

# Suspected Drug/Substance, non-Exclusive Drug Category



# Laboratory Testing

- Analytical Method Adaptation
- Analytes
- Validation
- CLIA
- Results
- Lessons Learned

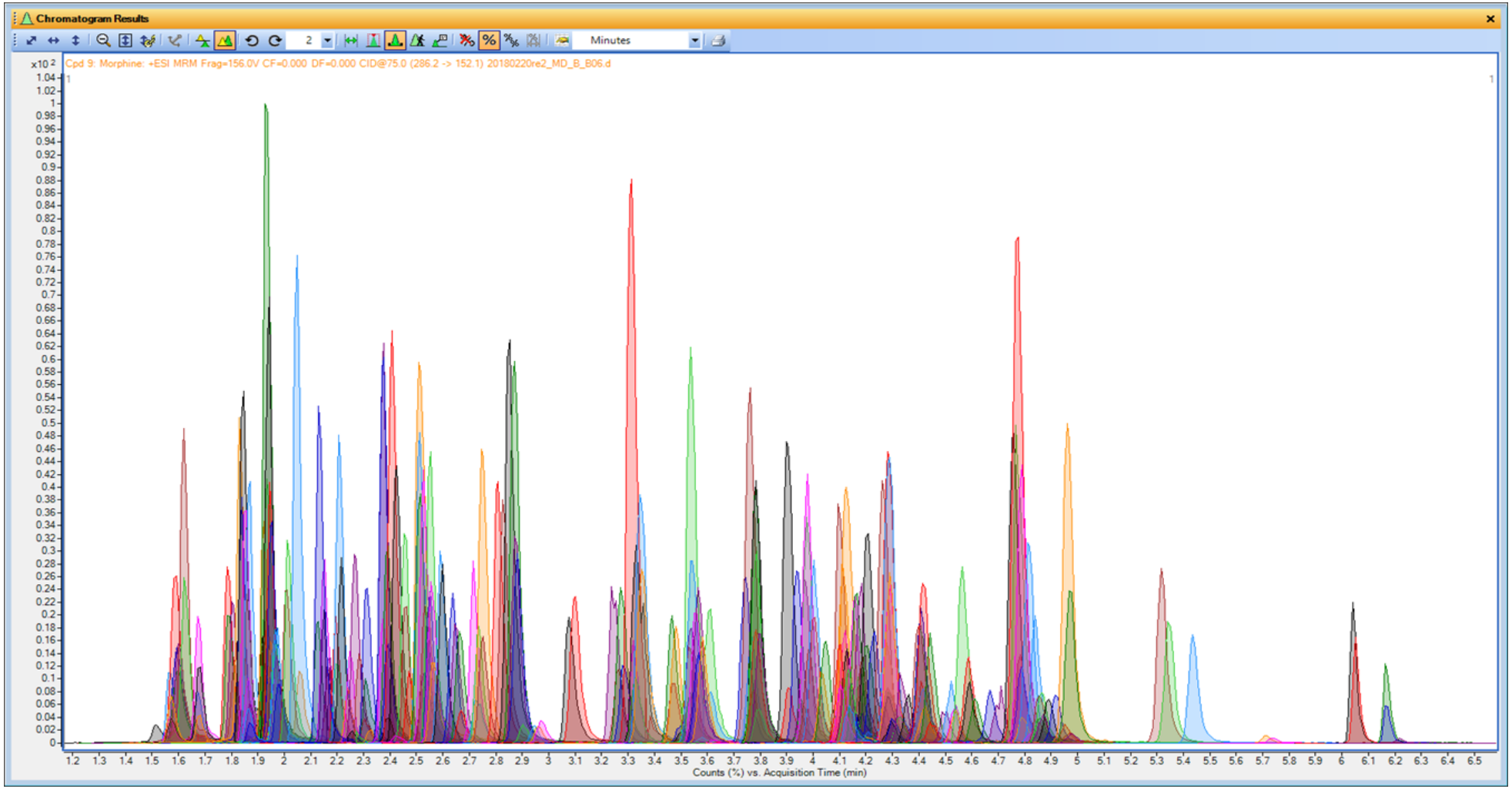
# Analytical Method

- Developed on an LC-QQQ (Agilent 6460) for qualitative (presence/absence) reporting
  - Matt Wogen developed internal analytical method. Adapted from PinPoint Testing LLC methodology.
- Blood and Urine matrices are validated
- Four calibrators and a single QC per compound, isotopically-labelled IS used when available
- Due to the large number of compounds and existing methodologies, 3 analytical methods were developed
  - Opioids (fentanyl and fentanyl-analogs) – 32 compounds (More being brought online)
  - Designer Drugs (e.g., synthetic cannabinoids, cathinones) – 68 compounds (More being brought online)
  - Multi-Drug Panel (e.g., stimulants, benzodiazepines, barbiturates, etc.) – 131 compounds

# Analytical Method

- Single sample clean-up procedure (SLE) for all three analytical methods (allows parallel processing), created Zephyr application for automation
- Urine preparation includes a 3 hour deconjugation step
- All three analytical methods use the same column (Phenomenex Kinetex Phenyl-Hexyl 50 x 2.1mm, 1.7µm) and mobile phases
- Dynamic (dMRM) acquisition mode (scheduled MRM)
  - Example - Multi-Drug Method: 246 MRMs/5 minutes, minimum dwell 3.44ms at 2 scans/sec

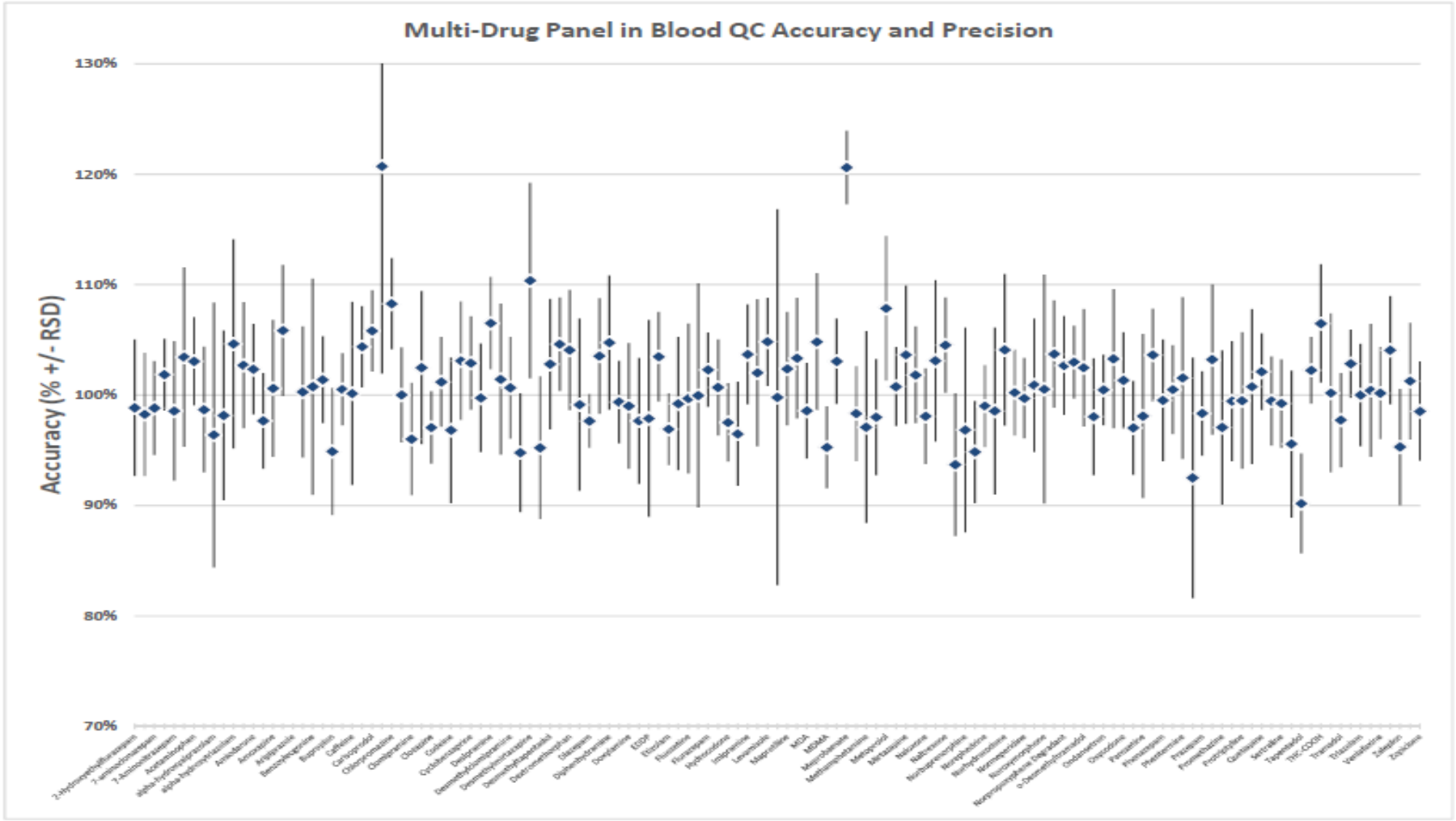
# Analytes


Chromatogram Results
Minutes
Cpd 9: Morphine: +ESI MRM Frag=156.0V CF=0.000 DF=0.000 CID@75.0 (286.2 -> 152.1) 20180220re2_MD_B_B06.d
x10 2
Counts (%) vs. Acquisition Time (min)

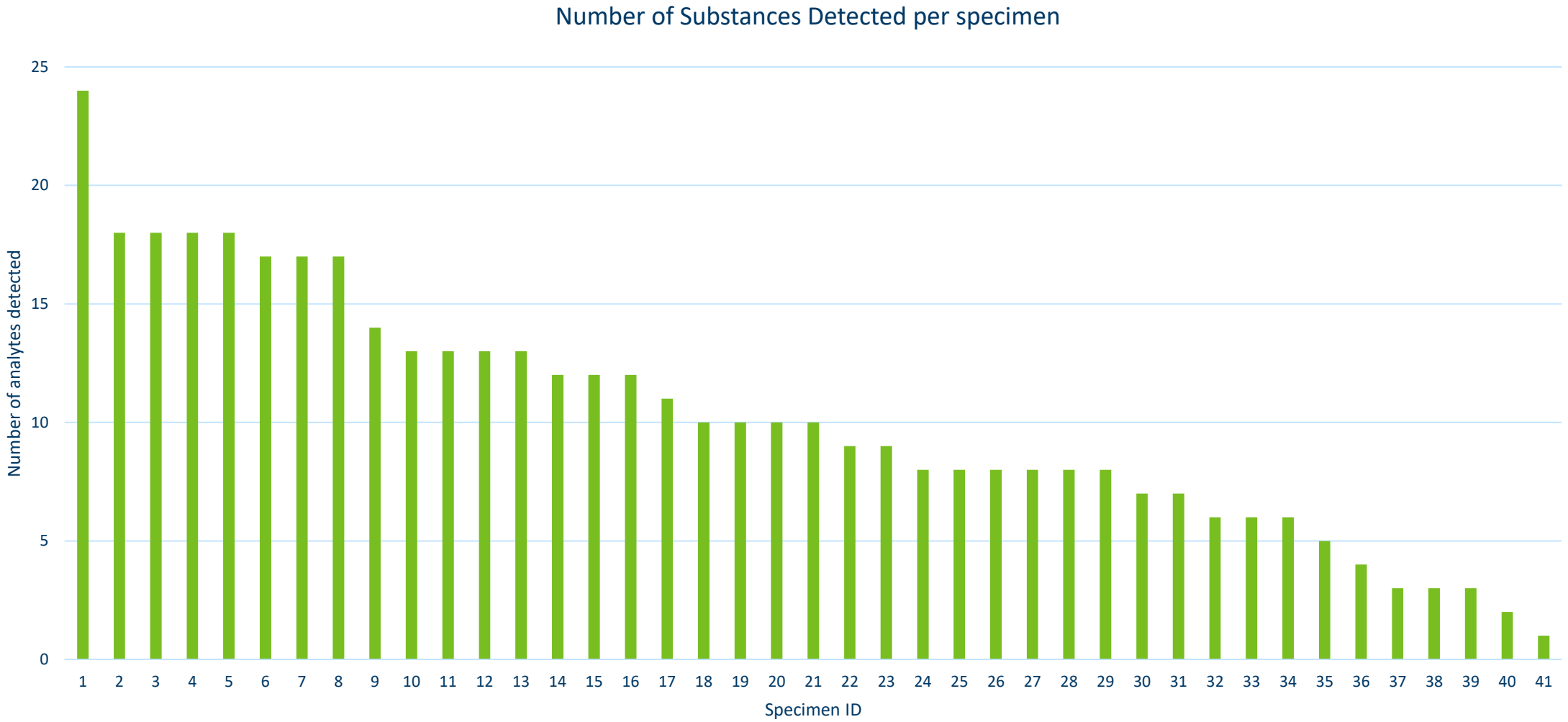
# CLIA Validation Followed

- Extraction recovery was consistent and sufficient to detect all compounds
- Generated a huge data set to process and review (100,000+ peaks)
- No false positives or false negatives
- Accuracy and precision were very good for most compounds
- Reporting limits established and verified based on low calibrator response

# Accuracy and Precision



# Results


Number of Substances Detected per specimen
Number of analytes detected
0
5
10
15
20
25
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41
Specimen ID

# Results

| Analyte | Lab Results | MNDOSA Report |
|---|---|---|
| **Caffeine** | 38 | -- |
| **Cotinine** | 39 | -- |
| | | |
| **Sympathomimetics** | 103 | 21 |
| Methamphetamine | 26 | 20 |
| Amphetamine | 27 | 1 |
| Norephedrine | 24 | |
| Pseudoephedrine | 21 | |
| Cocaine or Benzoylecgonine (BZE) | 4 | 3 |
| Methylphenidate | 1 | |
| MDMA | 0 | 1 |
| | | |
| **Opioids** | 62 | 10 |
| Heroin | 0 | 7* |
| Morphine | 13 | |
| Fentanyl or Norfentanyl | 12 | 1 |
| Oxymorphone or Noroxymorphone | 6 | |
| Buprenorphine or Norbuprenorphine | 6 | |
| Codeine | 6 | |
| Methadone or EDDP | 4 | 2 |
| Tramadol or o-Desmethyltramadol | 5 | 1 |
| Oxycodone or Noroxycodone | 2 | |
| Hydromorphone | 3 | |
| Acetyl Fentanyl or Acetyl Norfentanyl | 3 | |
| 6-MAM | 2 | |
| | | |
| **Benzodiazepines** | 49 | 6 |
| Lorazepam | 13 | |
| Midazolam or alpha-hydroxymidazolam | 13 | |
| Clonazepam or 7-aminoclonazepam | 8 | 1 |
| Oxazepam | 4 | |
| Alprazolam or alpha-hydroxyalprazolam | 4 | 2 |
| Temazepam | 2 | |
| Diazepam or Nordiazepam | 2 | 1 |
| Etizolam | 2 | 1 |
| Flurazepam | 1 | |

| Analyte | Positive Samples | MNDOSA Report |
|---|---|---|
| **Antidepressants** | 20 | 1 |
| Bupropion | 5 | 1 |
| Sertraline | 3 | |
| Venlafaxine or Desmethylvenlafaxine | 1 | |
| Citalopram | 1 | |
| Duloxetine | 3 | |
| Mirtazapine or Desmethylmirtazapine | 5 | |
| Nortriptyline | 1 | |
| Trazodone | 1 | |
| | | |
| **Antipsychotics** | 12 | 0 |
| Haloperidol | 7 | |
| Olanzapine or Desmethylolanzapine | 2 | |
| Clozapine | 1 | |
| Risperidone | 1 | |
| Aripiprazole | 1 | |
| | | |
| **THC-COOH** | 18 | 5 |
| | | |
| **Naloxone** | 7 | -- |
| | | |
| **Others** | | 0 |
| Diphenhydramine | 5 | |
| MCPP | 3 | |
| Dextromethorphan or Dextrorphan | 2 | |
| Atropine | 2 | |
| Ondansetron | 3 | |
| Amiodarone | 1 | |
| Metoprolol | 2 | |
| Ketamine or Norketamine | 1 | |
| Topiramate | 1 | |
| Buspirone | 1 | |
| Cyclobenzaprine | 1 | |
| Levamisole | 1 | |
| | | |
| **Synthetic cannabinoids or cathinones (e.g. "spice", "K2", "synthetics")** | 0 | 5 |

*of the 7 suspected heroin cases, 6 had fentanyl detected, including 2 where acetyl fentanyl was also detected. N = 41 Specimens analyzed.

# Current Challenges

- Lack of resources to facilitate the reporting of patients at the pilot hospitals.
- Efficient and successful transportation of samples from the hospitals to the lab can be expensive and challenging.
- Samples with high Methamphetamine concentrations have resulted in contamination of adjacent sample wells. Trying to identify when contamination happens so we can correct the issue.
- The number of desired drugs of abuse, metabolites, and adulterants keeps getting larger.
- A better strategy might be to use a targeted/non-targeted screening method (e.g., high resolution MS/MS or QTrap QQQ scan) for compound identification, and then follow-up with quantitation by a targeted LC-QQQ (or QTOF MRM-HR) method, if necessary.

# Acknowledgments


## MDH-PHL

- Joanne Bartkus
- Paul Moyer
- Stefan Saravia
- Matt Wogen
- Carin Huset
- Mark Lunda

## MDH – Injury Prevention

- Terra Wiens (Project Coordinator)
- Jon Roesler
- Mark Kinde
- Nate Wright

## MDH State Epidemiologist

- Ruth Lynfield

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# Thank you

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